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Editorial

Mycophenolate Mofetil Use for Inflammatory Bowel Disease

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EDITORIAL

Mycophenolate Mofetil (MMF) is a prodrug that gets converted to mycophenolic acid (MPA). MPA inhibits the Akt/mTOR and STAT5 pathways and has a reversible cytostatic effect on T and B lymphocytes [1].

MMF is FDA-approved for immunosuppressive therapy after solid organ transplantation. MMF has been used for multiple inflammatory/autoimmune conditions including psoriasis, dermatomyositis, autoimmune hepatitis, lupus erythematosus, myasthenia gravis, and Takayasu arteritis [2].

In this Editorial, we discuss the recently published systematic review and meta-analysis by Balassiano et al [3]. This systematic review and meta-analysis studied the use of MMF for the treatment of IBD patients. This review included both retrospective studies, case series, and clinical trials that evaluated the use of MMF in patients with IBD. Included patients were intolerant or unresponsive to Azathioprine. MMF was used in the included studies for induction and maintenance of remission, or as a steroid-sparing agent/immunomodulator. This study demonstrated MMF's efficacy in both induction and maintenance of remission in IBD patients. MMF was associated with added benefits for patients on steroids as well as those on anti-TNF therapy [3].

MMF has several boxed warnings in the United States, limiting its use outside FDA-approved indications. MMF should be prescribed only by healthcare providers experienced in immunosuppressive therapy and organ transplant management, with access to comprehensive laboratory and medical resources [4].

There is also a significant risk of infections associated with immunosuppression, including but not limited to opportunistic infections, which may result in significant morbidity and mortality. MMF use is associated with an increased risk of malignancy, including but not limited to lymphoma and skin cancers. There is also a boxed warning suggesting avoiding MMF use in pregnancy if alternative therapies are available, as its use is associated with congenital malformation and first-trimester pregnancy loss [5].

MMF has been associated with endoscopic findings that could be similar to acute colitis, IBD, ischemia, and graft-versus-host disease. Development of such side effects or endoscopic findings can lead to discontinuation of treatment, treatment interruption, or medication non-compliance [6, 7].

In this study, the pooled event rate for adverse events was 26.1% (20.3%-32.8%). The side effect profile is crucial in determining the role of MMF in IBD treatment. The IBD field is evolving around a patient-centered approach when it comes to therapeutic selection. IBDologists extensively discuss potential side effects and explore the patient's risk appetite. In general, more than one in four is considered a relatively high risk.

While side effects could constitute a major challenge for MMF use in IBD patients, their impact on treatment adherence, disease progression, and quality of life must be carefully weighed against MMF's potential benefits. The development of side effects has been associated with specific risk factors that increase the risk of developing side effects, which could open the door for drug adjustment and close monitoring that might allow its use. These risk factors include using a non-enteric-coated formulation, increased MMF blood levels, concomitant use of other immunosuppressant agents like calcineurin inhibitors, and female sex [8, 9, 10, 11].

MMF is relatively inexpensive compared to other IBD therapies. A dose price can range from as low as $0.32 for an oral dose to as high as $129.57 for an IV dose. This is cheaper compared to Azathioprine prices [12]. With the evolving widespread use of biosimilars, we are heading to an era with better accessibility to advanced IBD therapies, and this will allow gastroenterologists to adopt the recommended top-down approach in therapeutic selection [13].

The ACG guidelines for Crohn's disease recommend combining an immunomodulator with anti-TNF rather than using anti-TNF alone [14]. Hernandez-Camba et al. showed the added benefits of anti-TNF when combined with MMF [15]. This suggests potential benefits of MMF as an immunomodulator that could decrease anti-TNF immunogenicity and decrease the risk of secondary non-response.

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The study has some significant limitations. The included studies had heterogeneous designs. The study lacked a control group and did not compare MMF to alternatives such as Azathioprine or Mercaptopurine.

The IBD therapies are expanding, and it's an evolving field with multiple advancements annually. Selection of therapy in patients with IBD is a multistep and complex process that involves close consideration of the disease stage, patient population, disease complications, medication history, prognostic factors, presence of extra-intestinal manifestations of IBD, potential side effects of medications, patients' preferences, and cost implications [14].

In conclusion, this study highlights the potential benefits of MMF as a steroid-sparing agent or as an immunomodulator in conjunction with ant-TNF. It provides evidence for the use of MMF as an alternative for those intolerant or unresponsive to Azathioprine and Methotrexate.

Conflicts of Interest

The authors declare no competing interests that could have influenced the objectivity or outcome of this research

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Data Availability

The data that support the findings of this study are openly available, as cited in the article.

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